What is Claimed is:

A compound having the structure: 1.

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wherein R, R₀, and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldedyde linear or branched alkyl or cyclic acetal, fluorine, NR₁R₂, N-hydroximino, or N-alkoxyimino, wherein R₁ and R₂ are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R" is -CHY = CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3oxazolinyl, 3-indolyl or 6-indolyl; and wherein X is H, línear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; wherein Y is H or linear or branched chain alkyl; wherein Z is O, N(OR₃) or N-NR₄R₅, wherein R₃, R₄ and R_5 are independently H or a linear or branched alkyl; and wherein n is 0, 1, 2, or 3.

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The compound of claim 1 having the structure: 2.

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or

6 (CH₂)₃-OH.

A compound having the structure:

wherein R, R₀, and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldedyde linear or branched alkyl or cyclic acetal, fluorine, NR₁R₂, N-hydroximino, or N-alkoxyimino, wherein R₁ and R₂ are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R" is - CHY = CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; wherein Y is H or linear or branched chain alkyl; wherein Z is O, N(OR₃) or N-NR₄R₅, wherein R₃, R₄ and R₅ are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3.

4. The compound of claim 3 having the structure:

wherein R is H, methyl, ethyl, n-propyl, n-butyl or n-hexyl.

1 5. A compound having the structure:

wherein R, R_o, and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldedyde linear or branched alkyl or cyclic acetal, fluorine, NR₁R₂, N-hydroximino, or N-alkoxyimino, wherein R₁ and R₂ are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R" is - CHY = CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; wherein Y is H or linear or branched chain alkyl; wherein Z is O, N(OR₃) or N-NR₄R₅, wherein R₃, R₄ and R₅ are independently H or a linear or branched chain alkyl; and wherein n is 0, 1, 2, or 3.

6. The compound of claim 5 having the structure:

wherein R is H, methyl, ethyl, n-propyl, n-butyl, n-hexyl or hydroxypropyl.

A compound having the structure:

wherein R, R₀, and R' are independently H, linear or branched chain alkyl, optionally substituted by hydroxy, alkoxy, carboxy, carboxaldedyde linear or branched alkyl or cyclic acetal, fluorine, NR₁R₂, N-hydroximino, or N-alkoxyimino, wherein R₁ and R₂ are independently H, phenyl, benzyl, linear or branched chain alkyl; wherein R" is - CHY = CHX, or H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein X is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; wherein Y is H or linear or branched chain alkyl; wherein Z is O, N(OR₃) or N-NR₄R₅, wherein R₃, R₄ and R₅ are independently H or a linear or branched chain alkyl or alkoxy; and wherein n is 0, 1, 2, or 3.

8. A compound having the structure:

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9. A compound having the structure:

 wherein R' and R' are independently hydrogen, a linear or branched alkyl,

substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is oxygen, $(OR^*)_2$, $(SR^*)_2$, $-(O-(CH_2)_n-O)$ -, $-(O-(CH_2)_n-S)$ - or $-(S-(CH_2)_n-S)$ -; wherein R^* is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; wherein R_2B is a linear, branched or cyclic alkyl or substituted or unsubstituted aryl or benzyl boranyl moiety; and wherein n is 2, 3 or 4.

10. A compound having the structure:

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wherein R´ and R´´ are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is oxygen, $(OR^*)_2$, $(SR^*)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-(CH_2)_n-S)-$; wherein R* is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; wherein R₂B is a linear, branched or cyclic alkyl or substituted or unsubstituted aryl or benzyl boranyl moiety; wherein Y is OH, linear or branched chain alkoxy, trimethylsilyloxy, t-butyldimethylsilyloxy or methyldiphenysilyloxy; and wherein n is 2, 3 or 4.

11. A compound having the structure:

H OAC X OR'

wherein R' and R'' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is oxygen, $(OR)_2$, $(SR)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-CH_2)_n-C)-$

8 (CH₂)_n-S)-; and wherein n is 2, 3 or 4.

- 1 12. The compound of claim 11 wherein R' is TBS, R" is TPS and X is (OMe)₂.
- 13. A compound having the structure:

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wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is a halogen; wherein R" is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein Y is H or linear or branched chain alkyl.; wherein R' is H, linear or branched chain alkyl, hydroxymethyl, hydroxypropyl, alkyl carboxaldehyde, alkyl carboxaldehyde linear or cyclic acetal; and X is a halide.

- 1 14. The compound of claim 13 wherein R is acetyl and X is iodo.
- 1 15. A compound having the structure:

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- 3 4 5
- wherein R' and R'' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl,
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- alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is oxygen, $(OR)_2$, $(SR)_2$, $-(O-(CH_2)_n-O)-$, $-(O-(CH_2)_n-S)-$ or $-(S-CH_2)_n-CO-(CH_2)$
- 8 (CH₂)₀-
- (CH₂)_n-S)-; and wherein n is 2, 3 or 4.
- 1 16. A compo
- A compound having the structure:

wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein X is a halogen; wherein R' is H, linear or branched chain alkyl, alkyl carboxaldehyde, alkyl carboxaldehyde linear or cyclic acetal; wherein R" is H, linear or branched chain alkyl, phenyl, 2-methyl-1,3-thiazolinyl, 2-furanyl, 3-furanyl, 4-furanyl, 2-pyridyl, 3-pyridyl, 4-pyridyl, imidazolyl, 2-methyl-1,3-oxazolinyl, 3-indolyl or 6-indolyl; and wherein Y is H or linear or branched chain alkyl.

17. A compound having the structure:

wherein R is hydrogen, methyl, ethyl, n-propyl, n-hexyl, CO₂Et,

CH₂OH; or (CH₂)₃-OH; wherein R' and R'' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; and wherein Z is hydrogen, or linear or branched chain alkyl.

18. A method of preparing a Z-haloalkene ester having the structure:

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wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; wherein R' is hydrogen, methyl, ethyl, n-propyl, n-hexyl,

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, CH_2OH or $(CH_2)_3$ -OH; and wherein X is a halogen,

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which comprises

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(a) oxidatively cleaving a compound having the structure:

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under suitable conditions to form an aldehyde intermediate; and

(b) condensing the aldehyde intermediate with a halomethylene transfer agent under suitable conditions to form the Z-haloalkene ester.

- 19. The method of claim 18 wherein X is iodine.
- The method of claim 18 wherein the halomethylene transfer agent is Ph₃P=CR'l or (Ph₃P+CHR'l)I⁻¹
- 1 21. A method of preparing an optically pure compound having the structure:

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wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or 4 unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl 5

6 7 or benzoyl, which comprises: condensing an allylic organometallic reagent with an unsaturated (a)

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aldehyde having the structure:

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under suitable conditions to form an alcohol, and, optionally 11

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concurrently therewith, optically resolving the alcohol to form an

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optically pure alcohol having the structure:

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alkylating or acylating the optically pure alcohol formed in step (a) (b)

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under suitable conditions to form the optically pure compound.

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The method of claim 21 wherein the allylic organometallic reagent is an 22. allyl(trialkyl)stannane.

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- The method of claim 21 wherein the condensing step is effected using a reagent comprising a titanium tetraalkoxide and an optically active catalyst.
- The method of claim 23 wherein the optically active catalyst is S(-)BINOL.
- 1 25. A method of preparing an open-chain aldehyde having the structure:

wherein R° and R°° are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises:

(a) cross-coupling a haloolefin having the structure:

wherein R is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, triarylsilyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, and X is a halogen, with a terminal olefin having the structure:

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wherein $(OR''')_2$ is $(OR_0)_2$, $(SR_0)_2$, $-(O-(CH_2)_n-O)$ -, $-(O-(CH_2)_n-S)$ - or $-(S-(CH_2)_n-S)$ - where R_0 is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; and wherein n is 2, 3 or 4, under suitable conditions to form a cross-coupled compound having the structure:

wherein Y is CH(OR*)₂ where R* is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl; and deprotecting the cross-coupled compound formed in step (a) under suitable conditions to form the open-chain compound.

1 26. A method of preparing an epothilone having the structure:

which comprises:

(a) deprotecting a cyclized compound having the structure:

wherein R' and R' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, under suitable conditions to form a deprotected cyclized compound and oxidizing the deprotected cyclized compound under suitable conditions to form a desoxyepothilone having the structure:

and

(b) epoxidizing the desoxyepothilone formed in step (a) under suitable conditions to form the epothilone.

27. A method of preparing an epothilone precursor having the structure:

wherein R₁ is hydrogen or methyl; wherein X is O, or a hydrogen and OR'', each singly bonded to carbon; and wherein R₀, R' and R'' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises

(a) coupling a compound having the structure:

12 13 wherein R is an acetyl, with an aldehyde having the structure:

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wherein Y is oxygen, under suitable conditions to form an aldol intermediate and optionally protecting the aldol intermediate under suitable conditions to form an acyclic epthilone precursor having the structure:

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subjecting the acylic epothilone precursor to conditions leading to (b) 22 intramolecular olefin metathesis to form the epothilone precursor.

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The method of claim 27 wherein the conditions leading to intramolecular olefin 28. metathesis require the presence of an organometallic catalyst.

The method of claim 27 wherein the catalyst is a Ru or Mo complex. 29.

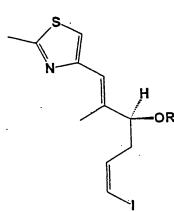
30. 1

A pharmaceutical composition for treating cancer comprising a compound of claim 1,

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- 2 3, 5, 7, or 8 and a pharmaceutically suitable carrier.
- 1 31. A method of treating cancer in a subject suffering therefrom comprising administering to the subject a therapeutically effective amount of a compound of claim 1, 3, 5, 7 or 8 and a pharmaceutically suitable carrier.
- 1 32. The method of claim 31 wherein the cancer is a solid tumor.
- 1 33. The method of claim 31 wherein the cancer is breast cancer.

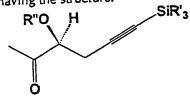
1 34. A method of preparing a Z-iodoalkene ester having the structure:



wherein R is hydrogen, a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises

(a) coupling a compound having the structure:

with a methyl ketone having the structure:



wherein R and R are independently a linear or branched alkyl,

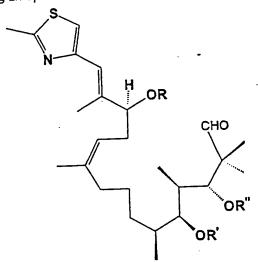
alkoxyalkyl, substituted or unsubstituted aryl or benzyl, under suitable conditions to form a compound having the structure:

treating the compound formed in step (a) under suitable conditions (b) to form a Z-iodoalkene having the structure:

and

deprotecting and acylating the Z-iodoalkene formed in step (b) under (c) suitable conditions to form the Z-iodoalkene ester.

A method of preparing an open-chain aldehyde having the structure: 35.



wherein R is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted

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aryloxyalkyl, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, triarylsilyl, linear or 5 branched acyl, substituted or unsubstituted aroyl or benzoyl; and wherein R' and 6 . R'' are independently hydrogen, a linear or branched alkyl, substituted or 7 unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or 8 branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises: 9 cross-coupling a haloolefin having the structure: (a) 10 11

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wherein X is a halogen, with a terminal hydroborane having the structure:

wherein R 2B is a linear, branched or cyclic alkyl or substituted or unsubstituted aryl or benzyl boranyl moiety; wherein Y is (OR₀)₂, (SR₀)₂, -(O-(CH₂)_n-O)-, -(O-(CH₂)_n-S)- or -(S-(CH₂)_n-S)- where R_0 is a linear or branched alkyl, substituted or unsubstituted aryl or benzyl; and wherein n is 2, 3 or 4, under suitable conditions to form a cross-coupled compound having the structure:

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and

- deprotecting the cross-coupled compound formed in step (a) under (b) suitable conditions to form the open-chain aldehyde.
- The method of claim 35 wherein R is acetyl; R' is TBS; R" is TPS; R*2B is derived 36. 1 from 9-BBN; and Y is (OMe)₂. 2
- A method of preparing a protected epothilone having the structure: 37. 1

OR" OR'

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wherein R' and R'' are independently hydrogen, a linear or branched alkyl, 4 substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkyl-arylsilyl, 5 alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or 6

benzoyl, which comprises: 7

monoprotecting a cyclic diol having the structure: (a)

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under suitable conditions to form a cyclic alcohol having the structure:

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- (b) oxidizing the cyclic alcohol formed in step (a) under suitable conditions to form the protected epothilone.
- 1 38. The method of claim 37 wherein R' and R'' are TBS.
- 1 39. A method of preparing an epothilone having the structure:

which comprises:

(a) deprotecting a protected cyclic ketone having the structure:

wherein R' and R' are independently hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, under suitable conditions to form a desoxyepothilone having the structure:

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and

- epoxidizing the desoxyepothilone formed in step (a) under suitable (p) conditions to form the epothilone.
- The method of claim 39 wherein R' and R'' are TBS. 40. 1
- A method of preparing a cyclic diol having the structure: 41. 1

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wherein R' is a hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl, which comprises:

cyclizing an open-chain aldehyde having the structure: (a)

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17 18 wherein R is a linear or branched alkyl, alkoxyalkyl, substituted or unsubstituted aryloxyalkyl, trialkylsilyl, aryldialkylsilyl, diarylalkylsilyl, triarylsilyl, linear or branched acyl, substituted or unsubstituted aroyl or benzoyl; and wherein Rinis a hydrogen, a linear or branched alkyl, substituted or unsubstituted aryl or benzyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, a linear or branched acyl, substituted or unsubstituted aroyl or benzoyl under suitable conditions to form an enantiomeric mixture of a protected cyclic alcohol having the structure:

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(b)

(c)

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said mixture comprising an α - and a β -alcohol component;

optionally isolating and oxidizing the α -alcohol formed in step (a) under suitable conditions to form a ketone and thereafter reducing the ketone under suitable conditions to form an enantiomeric mixture of the protected cyclic alcohol comprising substantially the β -alcohol; and

treating the protected cyclic alcohol formed in step (a) or (b) with a

deprotecting agent under suitable conditions to form the cyclic diol.

- 1 42. The method of claim 41 wherein R' is TBS and R'' is TPS.
- 1 43. A purified compound having the structure:
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R	H o c	ОН

wherein R is hydrogen, methyl, ethyl, propyl, hexyl, hydroxymethyl or
hydroxypropyl; wherein X is O; and wherein R₀, R' and R'' are independently

8 hydrogen or acetyl.

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1 44. A purified compound having the structure:

R₁

H O O ORO

ORO

OR'

wherein R₁ is hydrogen, methyl, ethyl, propyl, hexyl, hydroxymethyl or
hydroxypropyl; wherein X is O; and wherein R₀, R' and R' are independently
hydrogen or acetyl.

45. A composition comprising an amount of the compound of claim 1, 2, 3, 4, 5, 6, 7, 8, 43 or 44 effective to inhibit the growth of multidrug resistant cells and a

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pharmaceutically acceptable carrier. 3 The composition of claim 45, further comprising an amount of a cytotoxic agent. 46. 1 The composition of claim 46, wherein the cytotoxic agent is an anticancer agent. 47. 1 The composition of claim 47, wherein the anticancer agent is adriamycin. 48. 1 The composition of claim 47, wherein the anticancer agent is vinblastin. 49. 1 The composition of claim 47, wherein the anticancer agent is paclitaxel. 50. 1 The composition of claim 45, wherein the effective amount of the compound is 51. 1 between about 0.01 mg/kg to about 25 mg/kg of body weight. 2 A method of inhibiting the growth of multidrug resistant cells comprising contacting 52. 1 the multidrug resistant cells with an amount of the compound of claim 1, 2, 3, 4, 5, 2 6, 7, 8, 43 or 44 effective to inhibit the growth of multidrug resistant cells in 3 combination with a pharmaceutically acceptable carrier. 4 The method of claim 52, further comprising administering an amount of a cytotoxic 1 53. agent. 2 The method of claim 53, wherein the cytotoxic agent is an anticancer agent. 1 54. The method of claim 54, wherein the anticancer agent is adriamycin. 55. 1 The method of claim 55, wherein the anticancer agent is vinblastin. 56. 1 The method of claim 55, wherein the anticancer agent is paclitaxel. 1 5*7*. The method of claim 55, wherein the effective amount of the compound is between 58. 1 about 0.01 mg/kg to about 25 mg/kg of body weight. 2